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REMARKS

The Claim Amendments

Applicants acknowledge that claims 1-31 are pending in this application and that claims 22-25 and 30-31 are withdrawn from consideration.

Applicants have canceled claim 27 and added new claim 32.

Applicants have amended claims 1, 23-25, and 28.

Applicants have amended claim 1 to remove non-elected subject matter. Specifically, applicants have recited the phrase "W is selected from CH or CF" in place of the phrase "W is selected from nitrogen, CH, or CF".

Applicants have amended withdrawn claims 23-25 to recite the phrase "in a biological sample" in place of the phrase "in a biological sample or in a patient".

Applicants have canceled claim 27 and amended claim 28 to correct its dependency and to recite specific Gram-positive bacterial species namely; *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Enterococcus faecalis*, *Enterococcus faecium*, *Staphylococcus aureus*, *Coag. Neg. Staph*, *Bacillus anthracis*, and *Staphylococcus epidermidis*.

Applicants have added new claim 32 directed to a method of preventing a bacterial infection using compounds and compositions of the present invention. Support for this amendment is found in claim 27 and the specification at page 47, paragraph [00127] and page 48, paragraph [00134].

None of these amendments add any new matter.

The Reply to Restriction Requirement

Applicants filed a Reply (on October 9, 2006) to an Office Action (dated Sept. 15, 2006) setting forth a Restriction Requirement wherein applicants elected Group II with traverse. The Examiner found applicants arguments unpersuasive and maintained the restriction between Groups I or II and III based on radical W being CH of CF and W being nitrogen (see, Office Action ¶ 1, page 2). The Examiner's conclusion rested upon "newly available evidence" from a prior art document (see CA 93:39290) describing benzimidazol-2-yl carbamates as antifungal agents. Applicants acknowledge that the restriction requirement was deemed proper and is final. However, applicants respectfully disagree with the Examiner's conclusion. First, fungi and

bacteria are distinct classes of organisms (e.g., fungi are eukaryotic organisms whereas bacteria are prokaryotic organisms). Second, the benzimidazol-2-yl carbamate antifungal agents in CA 93:39290 are structurally dissimilar from the claimed compounds(e.g., no R^1 or Ring A substituents) such that one cannot draw any conclusion regarding the antibacterial activity of these antifungal agents. Therefore, the structure activity relationships cited in CA 93:39290 and relied upon by the Examiner to uphold the restriction requirement are improper. Accordingly, applicants retain the right to petition from the Examiner's finding that the requirement was proper and final.

Supplemental IDS

Applicants have also filed concurrently herewith a Supplemental IDS to cite the following co-pending applications: 10/883,995; 10/444,588 (US Publication No. US20040043989), 10/901,928 (US Publication No. US20050038247); 10/971,573 (US Publication No. US20050256136); and 10/986,569 (US Publication No. 20060025424). Additionally, applicants have cited U.S. Patent No. 6,632,809 which issued to applicants on October 14, 2003. The PCT published application WO 02/060879, corresponding to the issued U.S. patent No. 6,632,809, was cited in the IDS filed February 16, 2007 as is currently the subject of a reissue application, Serial No. 10/883,995.

The Rejections

35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 26-27 under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner contends that "claims 26-27 are ambiguous and confusing." Specifically, the Examiner contends that in claim 26, the phrase "decreasing bacterial quantity" renders the scope confusing as to whether this claim "treats infection or not." The Examiner suggests "decreasing the number of bacteria, if it does not affect the infective ability of the bacteria does not result in a patentable utility." Additionally, the Examiner contends that in claim 27, the term "preventing" and the phrase "lessening the severity of" are self-conflicting and confusing, respectively. Applicants traverse.

As discussed above, applicants have canceled claim 27 and recite the subject matter in part in amended claim 28 and new claim 32. Claim 28 recites methods of use of the compounds of the present invention for treating or lessening the severity of a bacterial infection. Specifically, applicants have recited the phrase "A method of treating or lessening the severity of" in place of the phrase "A method of treating, preventing, or lessening the severity of" in claim 28. Applicants have also recited only Gram-positive bacterial species in claim 28. Additionally, applicants have added new claim 32 directed to use of the compounds of the present invention for preventing certain Gram-positive bacterial infections. The use of antibiotics in the prevention or prophylaxis of bacterial infections is widely accepted and known to one of skill in the art. Specifically, antibiotics are often used prophylactically before a host of surgical and dental procedures to prevent post-operative or opportunistic infections (e.g., for surgical prophylactic use of antibiotics see, http://www.intmed.mcw.edu/drug/SurgProph.html and therein the use of antibiotics prior to upper GI and elective small bowel surgery, large bowel resections, acute appendectomy, penetrating abdominal trauma, hysterectomy, prostectomy, kidney, liver and pancreas transplantations, head and neck surgery, orthopaedic surgery, etc. and for dental prophylactic use of antibiotics for patients at risk for heart infections, see http://www.qualitydentistry.com/dental/information/abiotic.html). Thus, one skilled in the art would have the requisite assurance that the gyrase inhibitors/antibiotics of the present invention would have the asserted utility as prophylactic agents. Accordingly, applicants respectfully request that the Examiner withdraw this 35 U.S.C. § 112, second paragraph rejection.

Turning to claim 27, the method of "decreasing bacterial quantity in a patient" by administering a compound or composition of the present invention is both clear and unambiguous in its intended scope and utility. One of skill in the antimicrobial arts would readily understand that treating a bacterial infection with an antibiotic, such as a gyrase inhibitor, necessarily involves decreasing bacterial quantity in a patient. For instance, upon treatment with a suitable antibiotic, a patient typically experiences a decrease in bacterial number either by outright killing of the bacteria (a bactericidal effect) or by inhibiting growth and reproduction of the bacteria (a bacteriostatic effect). Thereafter, once the bacterial count has been sufficiently reduced, a patients' own immune system combined with the residual effect of the administered antibiotic "eliminate" the infection. Moreover, the compounds of the present invention inhibit

gyrase (see, e.g., Examples 27-29 at pages 83-85 and Exhibit A, Table 1A) and are batericidal and therefore would be expected to have the asserted utility of treating bacterial infections by decreasing bacterial quantity. Hence, one skilled in the arts would find the phrase "decreasing bacterial quantity" in claim 26 to be clearly directed towards a method of using a gyrase inhibitor of the present invention to treat a bacterial infection in a patient.

In sum, the scope and utility of claim 26 is clear and unambiguous as a method of treating a bacterial infection in a patient by decreasing bacterial quantity. Accordingly, applicants respectfully request that the Examiner withdraw this rejection.

35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 26-29 under 35 U.S.C. § 112, first paragraph "as failing to comply with the enablement requirement because the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." Specifically, the Examiner contends that "there is limited disclosure of the instantly claimed compounds being tested positive in an *S. aureus* MIC assay." The Examiner concludes that this is a scope of enablement rejection because "no enablement support for this one bacteria activity can be extrapolated to broad spectrum "antibacterial" activity." Applicants traverse in part.

In order to expedite prosecution, applicants have amended claim 28 to recite only Gram-positive bacterial species (namely *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Enterococcus faecalis*, *Enterococcus faecium*, *Staphylococcus aureus*, *Coag. Neg. Staph*, *Bacillus anthracis*, and *Staphylococcus epidermidis*). As discussed *infra*, applicants were enabled at the time of filing for the claimed methods of inhibition against the recited Gram-positive bacteria.

First, by way of reference to the *S. aureus* gyrase and topoisomerase IV ATPase and MIC assay and data provided in the specification (see, Examples 27-29 at specification pages 83-85), applicants demonstrated credible support for *S. aureus* utility (and Gram-positive utility generally). This MIC assay, as discussed in ¶ 6 of the §1.312 declaration by Paul S. Charifson filed herewith (hereinafter "the Charifson declaration"), is the most widely used and the industry gold standard for determining the *in vitro* antibacterial activity of a compound

Second, applicants have provided MIC data for *S. aureus* and two additional Gram-positive bacteria (see, Exhibit A, Table 1A and therein MIC data for selected compounds of the present invention, against *Streptococcus pneumoniae* and *Enterococcus faecalis*) as further evidence of Gram-positive activity for the claimed genus against Gram-positive organisms generally and against the recited organisms specifically. This additional MIC data provides further convincing evidence that the genus of compounds of the present invention inhibit Gram-positive organisms. As Charifson concludes, in ¶ 8 of his declaration, this MIC data provides compelling evidence that the compounds of the present invention inhibit Gram-positive organisms. Additionally, this data supports the claimed method of inhibiting Gram-positive bacteria in a patient and a method of treating a Gram-positive bacterial infection in a patient.

Third, in ¶ 9 of the Charifson declaration, Charifson provides scientific rationale to explain why one of skill in the antimicrobial arts would reasonably expect that a compound with demonstrated activity against three Gram-positive organisms (e.g. *S. aureus*, *S. pneumoniae*, and *E. faecalis*) would also be expected to be active against most other Gram-positive organisms. Charifson discusses the striking similarity amongst the gyrase and topoisomerase IV enzymes, especially in their respective active sites. Charifson further discusses similarity among Gram-positive bacteria with respect to their cell wall and permeability features. Finally, Charifson discusses how inhibiting the essential gyrase or topoisomerase enzymes inhibits DNA replication and leads to bacterial cell death. Further rationale presented by Charifson describes the broad spectrum of Gram-positive activity for an approved Gyrase inhibitor, Novobiocin, which binds in the same Gyrase B active site as the compounds of the present invention. Additionally, Charifson points to several other classes of approved antibiotics that also exhibit a broad spectrum of Gram-positive antibacterial activity.

In conclusion, based on the collection of antibacterial data in the specification as filed, the additional MIC data provided herewith confirming the data in the specification, the level of knowledge in the bacterial arts, and the scientific rationale provided in the Charifson Declaration, one of skill in the art would expect that the compounds of the present invention would have the claimed antibacterial activity against Gram-positive bacteria. As Charifson concludes in ¶ 10 of his Declaration, the MIC data presented herein, confirms that the gyrase inhibitors of the present invention were enabled at the time of filing for treating bacterial infections in patients.

Accordingly, applicants respectfully request that the Examiner withdraw this §112, first paragraph rejection.

Non-statutory Double Patenting

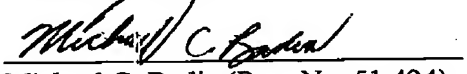
The Examiner has provisionally rejected claims 1-21 and 26-29 on the grounds of nonstatutory obviousness-type double patenting, as being unpatentable over claims 1, 2, 5, 23-26 of co-pending Application No. 10/459,420 (hereinafter the "'420 application"). The Examiner asserts that "although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are fully embraced by the copending claims because the instant claims are limited to the copending claims wherein R^3 is T-Ar, wherein T is $(CH_2)y$ and y is 0 compounds i.e. a ring moiety which is directly linked to the bicyclic core." Applicants respectfully traverse.

The '420 application does not teach, suggest or claim compounds wherein radical R^3 is $(CH_2)y$-RingA and y is 0. Thus, there are no overlapping R^3 moieties in these applications. Moreover, the '420 application discloses no compound species with the R^3 Ring A moieties of the present application. Therefore, contrary to the Examiner's assertion, the '420 application does not overlap with the instant application. Accordingly, applicants request that the Examiner withdraw this nonstatutory double patenting rejection.

Conclusion

Applicants request that the Examiner enter the above amendments, consider the accompanying remarks, and allow the pending claims to pass to issue.

Respectfully submitted,



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